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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Alexander Steinkasserer

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NORRIS, MCLAUGHLIN & MARCUS, PA
875 THIRD AVENUE
8TH FLOOR
NEW YORK, NY 10022

EXAMINER

JUEDES, AMY E

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/535,522	Applicant(s) STEINKASSERER ET AL.	
	Examiner AMY E. JUEDES	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-33,35-39,46,49-51 and 53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-33,35-38,46,49-51 and 53 is/are rejected.
- 7) ☒ Claim(s) 39 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input checked="" type="checkbox"/> Other: <u>notice to comply</u> . |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :7/23/09, 9/4/08, 9/16/05, 5/18/05.

DETAILED ACTION

1. Applicant's amendment, filed 8/17/09, is acknowledged.

Claims 34, 40-45, 47-48, and 52 have been cancelled.

Claims 29, 33, 35, and 39 have been amended.

Claim 53 has been added.

Claims 29-33, 35-39, 46, 49-51, and 53 are pending.

Applicant's election with traverse of group I, drawn to a monomeric CD83 protein, claims 29-39, 46, and 53, in the reply filed on 8/17/09 is acknowledged.

Applicant's traversal is on the grounds that the amended claims are characterized by unity of invention. Applicant's argument is persuasive, and the restriction requirement is withdrawn

Claims 29-33, 35-39, 46, 49-51, and 53 are under examination.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) set forth below:

The sequence "Gly-Ser-Pro-Gly" recited in claim 53 and on page 13 of the specification is not present in the CRF or sequence listing. A new sequence listing, CRF, and statement that the two are identical are required.

Furthermore, the specification should be amended to indicate the SEQ ID No: for the sequences disclosed in Figure 1 and 8.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

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Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

4. Claim 38 is object to for the following informalities: For clarity, it is suggested to amend claim 38 such that it reads a "protein wherein the fifth cysteine residue, corresponding to residue 129 of SEQ ID NO: 2 or residue 114 of SEQ ID NO: 8, is substituted".

5. Claims 39 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Claim 32 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 32 recites that the C-terminus of the protein comprises one or more additional amino acid residues derived from the neighboring intracellular domain. This might encompass a CD83 protein consisting of residues 20 to 149 of SEQ ID NO: 2, for example. However, said CD83 protein would not read on independent claim 29. A proper dependent claim shall not conceivably be infringed by anything which would not also infringe the basic claim.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 32-33, 35-38, 46, 49-51, and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "small" in claims 29, 33, 35, and 53 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does

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not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, tyrosine is "small" compared to tryptophan, but might not be considered "small" compared to glycine. Thus, the scope of a claim directed to substitution with a "small" amino acid cannot be established.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 53 is rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A monomeric soluble CD83 consisting of amino acid residues 1 to 130 of SEQ ID NO:8, having the additional amino acid residues Gly-Ser-Pro-Gly at the N-terminus.

It is noted that applicant has not cited any support for the new limitation in the specification.

A review of the specification fails to reveal support for the new limitations.

At page 13, the specification discloses soluble CD83 proteins comprising at least amino acids 20 to 145 of SEQ ID NO: 2, and derivatives such as those carrying at their N-terminus a short functional peptide (Gly-Ser-Pro-Gly). Thus, the specification provides support for a monomeric CD83 consisting of amino acid residues 20 to 145 of SEQ ID NO: 2, having the additional amino acid residues Gly-Ser-Pro-Gly at the N-terminus. However, residues 1 to 130 of SEQ ID NO: 8 represent said sequence (i.e.

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residues 20 to 145 of SEQ ID NO: 2 plus the amino acid residues Gly-Ser-Pro-Gly at the N-terminus). Thus, the instant claim encompasses a soluble CD83 protein having two repeats at the N-terminus. The specification does not disclose a CD83 protein comprising two repeats of the Gly-Ser-Pro-Gly sequence at the N-terminus, as now claimed.

10. Claims 29-33, 35-37, 46, 49-51, and 53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A monomeric soluble form of CD83 consisting of amino acid residues 20 to 145 of SEQ ID NO: 2 or consisting of amino acid residues 1 to 130 of SEQ ID NO: 8, wherein the fifth cysteine residue (i.e. residue 129 and 114, respectively) is substituted, and a method of treating multiple sclerosis comprising administering said monomeric soluble form of CD83

does not reasonably provide enablement for:

A monomeric soluble form of CD83 consisting of amino acid residues 20 to 145 of SEQ ID NO: 2 or consisting of amino acid residues 1 to 130 of SEQ ID NO: 8, wherein the one or more cysteine residues are substituted, and a method for treating or preventing a disease with said monomeric soluble form of CD83.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

“The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art.” *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The “amount of guidance or direction” refers to that information in the application, as originally filed,

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that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)” The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable one skilled in the art to make and use the soluble CD83 proteins as broadly claimed. The instant claims are drawn to a soluble CD83 protein consisting of amino acid residues 20 to 145 of SEQ ID NO: 2 or residues 1 to 130 of SEQ ID NO: 8, wherein or more cysteine residues are substituted. It is noted that the claims do not specify any functional requirement of the claimed CD83 polypeptides. The recited sequences comprise 5 cysteine residues. The instant claims encompass proteins comprising mutations of up to all 5 cysteine residues. Cysteine residues play an important role in the structure and function of proteins, and many proteins simply cannot form stable native structures without a disulphide bond between cysteine residues (see Thangudu et al., 2007). Furthermore, it is known that even a single cysteine substitution can dramatically effect the function of proteins (See Zhong et al., 2006). The instant specification on page 21-22 discloses that the monomeric soluble CD83 proteins of the invention are useful for binding and causing disruption in the binding of dendritic cells to T cells, particularly in pharmaceutical formulations. However, given the importance of cysteine residues in the structure and function of proteins, it would be extremely unpredictable as to whether even a single cysteine substitution (much less more than one) would result in a protein with the same structure and function of wild type CD83 protein. The instant specification demonstrates that a CD83 protein consisting of residues 20 to 145 of SEQ ID NO: 2, wherein a single cysteine at position 129 has been substituted with another amino acid residue functions to inhibit dendritic cell/T cell interaction. SEQ ID NO: 8 of the instant application represents the sequence of residues 20 to 145 of SEQ ID NO: 2, including a peptide linker at the N-terminus. Thus, the specification demonstrates that

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substitution of the fifth cysteine residue of amino acids 20 to 145 of SEQ ID NO: 2 or residues 1 to 130 of SEQ ID NO: 8 (i.e. residues 129 and 114, respectively) results in a functional protein. However, the specification does not provide any guidance as to the overall structure of CD83, including the presence of cysteine disulphide bonds that might be critical for structure/function. Furthermore, the instant specification does not provide any guidance regarding the use of other CD83 proteins in which up to all 5 cysteine residues have been substituted. Said CD83 proteins would not likely share the same structure as the CD83 of SEQ ID NO: 2, nor would they likely be capable of binding and disrupting dendritic cell/T cell interactions. Thus, given the breadth of the claims, the unpredictability of the art, and the lack of guidance by the instant specification, one skilled in the art would not be able to make and use the CD83 proteins as broadly claimed.

Furthermore, claims 49-51 are drawn to methods of treatment employing the monomeric CD83 proteins. As noted above, it would be extremely unpredictable as to whether any cysteine substitution, including multiple cysteine substitutions, would result in a functional CD83 protein. Therefore, for the same reasons set forth above, it would require undue experimentation to use the monomeric CD83 proteins, as broadly claimed in claim 29, for treatment methods which would require a structurally and functionally intact soluble protein. Additionally, even if the claims were limited to monomeric CD83 proteins with a cysteine substitution at residue 129 of SEQ ID NO:2 or 114 of SEQ ID NO: 8, claims 49-50 still encompass treating a wide range of disease with different etiologies and pathological mechanisms. For example, claim 49 encompasses treatment of disease caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells, or B cells. This might encompass treating diseases including cancer, autoimmune disease, congenital immunodeficiencies, and infections. The ability of a single treatment to be effective for such diverse diseases is extremely unpredictable. For example, immune deficiencies, cancer, and infection typically involve enhancing the T cell immune response. However, the instant specification demonstrates that soluble CD83 suppresses T cell responses. Thus, it is not clear how this would be effective for treating infections (including AIDS),

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immune deficiencies, or cancer, as is encompassed by the instant claims. Additionally, even if the claims were limited to conditions in which it is sometimes desirable to inhibit T cells (for example in some autoimmune diseases), the treatment method of the claims would still be highly unpredictable. For example, even in autoimmune disease, a therapy that benefits one autoimmune disease will sometimes make another disorder worse (see Progress in Autoimmune Diseases Research, 2005, page 55, of record). Additionally, the instant claims encompass not only treatment, but prevention of disease. Given its broadest reasonable interpretation, the term prevention encompasses a complete prevention such that no signs or symptoms of disease ever develop. Thus, based on the unpredictability of the art and the breadth of the claims, the instant specification must provide a sufficient an enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that soluble CD83 is effective for treating, but not completely preventing EAE, an art recognized animal model of multiple sclerosis. However, this is not commensurate in scope with the instant claims. Thus, given the breadth of the claims, the unpredictability of the art, and the lack of guidance provided by the instant specification, it would require undue experimentation to practice the claimed invention.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy E. Juedes

Patent Examiner

Technology Center 1600

/Amy E. Juedes/

Patent Examiner, Art Unit 1644